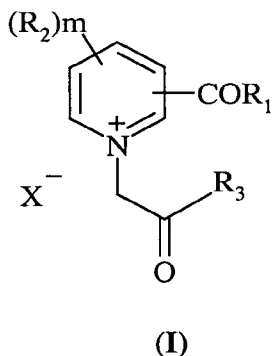


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A cosmetic composition comprising an effective amount of a compound with free radical scavenging, preformed AGE breaking and AGE-formation inhibiting activity having the formula (I),



or its cosmetically acceptable salts contained in a cosmetically acceptable carrier
wherein

R_1 is $-N(R_7)N(R_7)R_9$;

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

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m is 0, 1 or 2;

R₃ is selected from the group consisting of R₇, OR₇, N(R₇) (R₁₀), N=C(R₇) (R₁₀), N(R₇)N(R₇) (R₁₀), N(R₇) N=C(R₇) (R₁₀) and CH(R₇)C(O)R₈

where R₈ is selected from the group consisting of R₇, OR₇ and NR₇R₁₀;

R₉ is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, C(O)R₁₀, -SO₂R₁₀, C(S)NHR₁₀, C(NH) NH (R₁₀) and C(O) NHR₁₀;

R₁₀ is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R₇, provided R₁₀ may be the same or different

for R₁ and R₃ in the same compound;

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF₄⁻ and PF₆⁻;

wherein the heteroaryl as defined for R₃ and R₁₀ has heteroatoms selected from the group consisting of O, N and S, wherein the heteroaryl may be substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, C₁-C₆ straight chain or branched alkyl group, and nitro-group;

with proviso that,

- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl

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- (iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen, and
- (v) at least one heteroaryl group is present.

2. (original) The composition as claimed in claim 1, wherein $-C(O)R_1$ group of said compound is at position 3 or 4.

3. (original) The composition as claimed in claim 2, wherein $-C(O)R_1$ group of said compound is at position 3.

4. (previously presented) The composition as claimed in claim 1, wherein for said compound m is 0 or 1.

5. (previously presented) The composition as claimed in claim 2, wherein for said compound m is 0 or 1.

6. (previously presented) The composition as claimed in claim 3, wherein for said compound m is 0 or 1.

7. (previously presented) The composition as claimed in claim 1, wherein for said compound m is 0.

8. (previously presented) The composition as claimed in claim 2, wherein for said compound m is 0.

9. (previously presented) The composition as claimed in claim 3, wherein for said compound m is 0.

10. (previously presented) The composition as claimed in claim 1, wherein for said compound X is a halide ion.

11. (previously presented) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of:

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and
- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

12. (previously presented) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of:

- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and
- (x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

13. (previously presented) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of :

- (aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or

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other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

14. (previously presented) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-

[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

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(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine

dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine

dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium

bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride

or other cosmetically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or

other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide

or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium

bromide or other cosmetically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

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chloride or other cosmetically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]

hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

- B1
cont.*
- 15. (cancelled)
 - 16. (currently amended) The composition as claimed in claim 1, which is suitable for
 - a) reversing and ~~preventing~~ delaying the onset of wrinkles,
 - b) reversing and ~~preventing~~ delaying the onset of fine lines,
 - c) promoting epidermal growth,
 - d) photo protection,
 - e) reversing and ~~preventing~~ delaying the onset of skin discoloration,
 - f) reversing and ~~preventing~~ delaying the onset of age spots,
 - g) conditioning and ~~preventing~~ delaying the onset of dryness,
 - h) reversing and ~~preventing~~ delaying the onset of stretch marks,
 - i) reversing and ~~preventing~~ delaying the onset of blemishes,
 - j) skin care/ skin conditioning,
 - k) reversing and ~~preventing~~ delaying the onset of senile xerosis,
 - l) conditioning and ~~preventing~~ delaying the onset of sun burns,

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- Bi
cont
- m) preventing and reversing the loss of collagen,
 - n) improving skin texture,
 - o) improving skin tone,
 - p) enhancing of skin thickness,
 - q) decreasing pore size,
 - r) restoring skin luster,
 - s) minimizing signs of fatigue,
 - t) reducing acne,
 - u) treatment of Telangiectasia or
 - v) improving the aesthetic appearance of hair and nails.

17. (cancelled)

18. (currently amended) The composition as claimed in claim-17 16, in the form of a solution, gel, ointment, lotion, cream, microemulsion aerosol, dispersion or milk.

19. (currently amended) A method of cosmetic application with reversing and ~~preventing effects on~~ delaying the onset of aging and wrinkling of the skin comprising applying an effective amount of a cosmetic composition comprising said compound with free radical scavenger, AGE-breaker and AGE formation-inhibitor activity having the formula (I) as defined in Claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

20. (original) The method as claimed in claim 19, wherein the effective amount is effective for ageing.

21. (original) The method as claimed in claim 20, wherein aging is extrinsic aging

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and intrinsic aging.

22. (original) The method as claimed in claim 20, wherein aging is extrinsic aging.

23. (currently amended) A method of cosmetic application with reversing and ~~preventing effects on~~ delaying the onset of at least one of the following :

- B1 cont.*
- i) fine lines,
 - ii) skin discoloration
 - iii) age spots
 - iv) stretch marks
 - v) blemishes and
 - vi) senile xerosis
 - vii) ~~preventing~~ delaying the onset of and reversing loss of collagen

comprising applying an effective amount of a cosmetic composition comprising said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

24. (currently amended) A method of cosmetic application with conditioning and ~~preventing effects in~~ delaying the onset in skin dryness and /or sun burns comprising applying an effective amount of a cosmetic composition comprising said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or cosmetically acceptable salts thereof contained in a cosmetically acceptable carrier.

25. (previously presented) A method of cosmetic application with effects of

promoting epidermal growth and/or photo protection, improving skin texture, improving skin tone, enhancing skin thickness, decreasing pore size, restoring skin luster, minimizing signs of fatigue, reducing tone, treatment of telangiectasia comprising applying an effective amount of a cosmetic composition comprising said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

26. (previously presented) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

- B1 cont*
- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,
 - (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,
 - (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,
 - (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and
 - (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

27. (previously presented) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium

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bromide or other cosmetically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

28. (previously presented) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

29. (previously presented) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable

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salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

B¹ cont.
(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or

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other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

30. (cancelled)

31. (previously presented) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien -2'- yl -2-oxoethyl) -3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy -2-oxoethyl) -3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other

pharmaceutially acceptable salts thereof,

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

32. (previously presented) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

33. (previously presented) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

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(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and
(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

34. (previously presented) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride

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or other cosmetically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

35. (cancelled)

36. (previously presented) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,

B₁ cont (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

37. (previously presented) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

38. (previously presented) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

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(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

39. (previously presented) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts

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thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

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- (bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,
- (bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and
- (bi) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

B1
cont-
40. (cancelled)

41. (previously presented) The method as claimed in claim 25, wherein said compound is selected from the group consisting of the following compounds:

- (a) N,N'-bis[3-carbonyl-1-(2-thien -2'- yl -2-oxoethyl) -3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,
- (b) 1-(2-ethoxy -2-oxoethyl) -3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,
- (f) 1-(2-thien -2'-yl -2-oxoethyl) -3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and
- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

42. (currently amended) The method as claimed in claim 25, wherein said compound is selected from the group consisting of the following compounds:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

43. (currently amended) The method as claimed in claim 25, wherein said compound is selected from the group ~~consisting~~ consisting of the following compounds:

B1 cont.
(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl)-pyridinium chloride or other cosmetically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

44. (currently amended) The method as claimed in claim 25, wherein said compound

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is selected from the group ~~containing~~ consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

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(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

By cont. (bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

45. (cancelled)

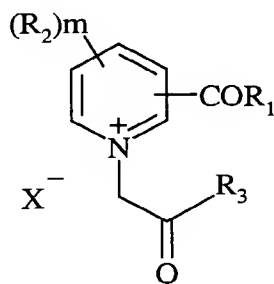
46. (original) The cosmetic composition as claimed in claim 1, wherein the concentration of said compound is between 0.005 to 50% by weight.

47. (original) The cosmetic composition as claimed in claim 26, wherein the concentration of said compound is between 0.25% to 5.0% by weight.

48. (original) A cosmetic composition comprising the compound of the Formula (I) as defined in claim 1 or other cosmetically acceptable salts thereof and one or more agents selected from the group consisting of: emollients, emulsifiers, agents modifying skin differentiation and/or proliferation and/or pigmentation, antiparasitic agents, preservatives, alcohols, fragrances, thickening agents, humectants, colorants, silicones, exfoliating agents, keratolytic agents, retinoids, sunscreens, skin penetration enhancers, anti-inflammatory agents, vitamins, thrombolytic agents, anticlotting agents, capillary protectants, additional antioxidants, hormones, antibacterial agents, antiviral agents, steroidal anti-inflammatory agents, anaesthetics, anti-seborrhoeic agents, anti-dandruff agents, anti-acne agents, anti-free radical agents, analgesics, lipophilic compounds, antihistamine agents, insect repellants, skin cooling compounds, lubricants and anti-fungal agents or mixtures thereof.

49. (previously presented) A method of cosmetic application comprising applying an effective amount of said composition as claimed in claim 48.

50. (currently amended) A pharmaceutical composition for scavenging free radicals in the body cell of a mammal comprising a compound of formula (I) or pharmaceutically acceptable salts thereof



(I)
25

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in admixture with pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

R_1 is $-N(R_7)N(R_7)R_9$,

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including
heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2
alkyl and SO_2 aryl;

B₁ cont.
 m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$, $N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$,
 $-SO_2R_{10}$, $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each
case may be the same or different from substituent R_7 , provided R_{10} may be the same or different
for R_1 and R_3 in the same compound;

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion,
oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion,
phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- and PF_6^- ;

wherein the heteroaryl as defined for R₃ and R₁₀ has heteroatoms selected from the group consisting of O, N and S, wherein the heteroaryl may be substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, C₁-C₆ straight chain or branched alkyl group, and nitro group;

with proviso that,

- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl;
- (iv) when R₃ is OR₇, R₁ is N(R₇)N(R₇)R₉ and R₉ is C(O)R₁₀ where R₁₀ is alkyl, then R₇ is not hydrogen; and
- (v) at least one heteroaryl group is present.

51. (original) The composition as claimed in claim 50, wherein -C(O)R₁ group of said compound is at position 3 or 4.

52. (original) The composition as claimed in claim 51, wherein -C(O)R₁ group of said compound is at position 3.

53. (previously presented) The composition as claimed in claim 50, wherein for said compound m is 0 or 1.

54. (previously presented) The composition as claimed in claim 51, wherein for said compound m is 0 or 1.

55. (previously presented) The composition as claimed in claim 52, wherein for said

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compound m is 0 or 1.

56. (previously presented) The composition as claimed in claim 50, wherein for said compound m is 0.

57. (previously presented) The composition as claimed in claim 51, wherein for said compound m is 0.

58. (previously presented) The composition as claimed in claim 52, wherein for said compound m is 0.

59. (previously presented) The composition as claimed in claim 50, wherein for said compound X is a halide ion.

B1 cont.
60. (previously presented) The composition as claimed in claim 50 wherein said compound is selected from the group consisting of

(a) N,N'-bis[3-carbonyl-1-(2-thien -2'- yl -2-oxoethyl) -3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(b) 1-(2-ethoxy -2-oxoethyl) -3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,

(f) 1-(2-thien -2'-yl -2-oxoethyl) -3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

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61. (previously presented) The composition as claimed in claim 50 wherein said compound is selected from the group consisting of:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

62. (currently amended) The composition as claimed in claim 50 wherein said compound is selected from the group ~~consisting~~ consisting of:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof.

63. (previously presented) The composition as claimed in claim 50 wherein said

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compound is selected from the group consisting of:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

But count
(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

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(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other pharmaceutically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

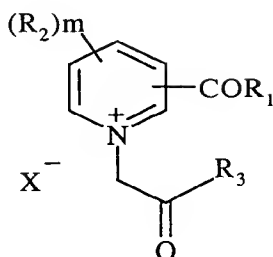
(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

64. (cancelled)

65. (currently amended) A method of scavenging free radical in the body cells comprising administering to a mammal in need of scavenging free radical from its body cells an effective amount of a compound of formula (I) or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier, diluent, excipient or solvent,



wherein

R_1 is $-N(R_7)N(R_7)R_9$;

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$, $N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, $-SO_2R_{10}$, $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different

for R_1 and R_3 in the same compound;

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- and PF_6^- ;

wherein the heteroaryl as defined for R_3 and R_{10} has heteroatoms selected from the group consisting of O, N and S, wherein the heteroaryl may be substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, C_1 - C_6 straight chain or branched alkyl group, and nitro group;

with proviso that,

- B1 cont.*
- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
 - (ii) the nitrogen of heteroaryl ring of R_{10} , when present, may be quaternized;
 - (iii) when R_3 is OR_7 and R_1 is $-NHNH_2$ then R_7 is not alkyl;
 - (iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and
 - (v) at least one heteroaryl group is present.

66. (previously presented) The method as claimed in claim 65, wherein said compound is selected from the group consisting of:

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl)-2-oxoethyl]-3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other

pharmaceutically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

67. (previously presented) The method as claimed in claim 65, wherein said compound is selected from the group consisting of:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

68. (previously presented) The method as claimed in claim 65, wherein said compound is selected from the group consisting of:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

- (af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,
- (ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof, and
- (am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof.

69. (previously presented) The method as claimed in claim 65 wherein said compound is selected from the group consisting of:

- B1 cont.* (an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium

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bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other pharmaceutically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or
other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide
or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium
bromide or other pharmaceutically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
chloride or other pharmaceutically acceptable salts thereof,

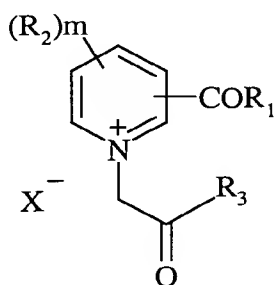
(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]
hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other
pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium
bromide or other pharmaceutically acceptable salts thereof.

70. (cancelled)

71. (currently amended) A method of treating diseases caused by accumulation of
free radicals in the body cells of a mammal comprising treating a mammal affected by such
disease with an effective amount of a compound of formula (I)



(I)

or its pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, diluent,
excipient or solvent,

wherein

R_1 is $-N(R_7)N(R_7)R_9$;

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including
heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2
alkyl and SO_2 aryl;

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m is 0, 1 or 2;

R₃ is selected from the group consisting of R₇, OR₇, N(R₇) (R₁₀), N=C(R₇) (R₁₀),
N(R₇)N(R₇)(R₁₀), N(R₇) N=C(R₇) (R₁₀) and CH(R₇)C(O)R₈

where R₈ is selected from the group consisting of R₇, OR₇ and NR₇R₁₀;

R₉ is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, C(O)R₁₀,
-SO₂R₁₀, C(S)NHR₁₀, C(NH) NH (R₁₀) and C(O) NHR₁₀;

R₁₀ is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each
case may be the same or different from substituent R₇, provided R₁₀ may be the same or different
for R₁ and R₃ in the same compound;

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion,
oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion,
phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF₄⁻ and PF₆⁻;

*B!
cont*

wherein the heteroaryl as defined for R₃ and R₁₀ has heteroatoms selected from the group
consisting of O, N and S, wherein the hetroaryl may be substituted with one or more substituents
selected from the group consisting of F, Cl, Br, I, C₁-C₆ straight chain or branched alkyl group,
and nitro group;

with proviso that,

(i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked
together to form a cyclic structure;

(ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;

(iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl;

(iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and

(v) at least one heteroaryl group is present,

wherein the diseases caused to be treated are selected from the group consisting of:

- B!
cont.*
- a) Neurodegenerative diseases selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, Motor neuron disease and Prion disease,
 - b) Diabetes and Diabetic Vascular Complications,
 - c) Intestinal Diseases,
 - d) Liver Diseases,
 - e) Cancer diseases selected from the group consisting of lung cancer, colorectal cancer, cervical cancer, breast cancer and malignant melanoma,
 - f) Cardiac Diseases,
 - g) Ophthalmic Disorders,
 - h) HIV Disease,
 - i) Respiratory Disease, and
 - j) Renal Diseases.

72. (previously presented) The method as claimed in claim 71 wherein said compound is selected from the group consisting of:

- (a) N,N' -bis[3-carbonyl-1-(2-thien-2'-yl)-2-oxoethyl]-3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other

pharmaceutically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof.

73. (previously presented) The method as claimed in claim 71 wherein said compound is selected from the group consisting of:

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

74. (previously presented) The method as claimed in claim 71 wherein said compound is selected from the group consisting of:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride or other pharmaceutically acceptable salts thereof, and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof.

75. (previously presented) The method as claimed in claim 71 wherein said compound is selected from the group consisting of:

By Cont. (an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine

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dichloride or other pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other pharmaceutically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

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(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

76. (cancelled)

77. (previously presented) The pharmaceutical composition as claimed in claim 50 in the form of an oral formulation, wherein the carrier, diluent, excipient or solvent is one acceptable for oral administration.

78. (original) The pharmaceutical composition as claimed in claim 50 wherein said acceptable carrier, diluent, solvent or excipient is selected from the group consisting of starch, lactose, polyvinyl pyrrolidone (K-30), talc and magnesium stearate.

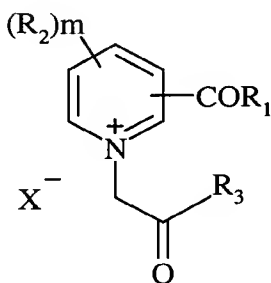
79. (previously presented) The pharmaceutical composition as claimed in claim 50 in the form of a parenteral formulation, wherein the carrier, diluent, excipient or solvent is one acceptable for parenteral administration.

80. (original) A method for the preparation of a parenteral formulation as claimed in claim 79 which comprises dissolving one or more compounds represented by general formula (I), as defined in claim 50, in polyethylene glycol 400 and diluting the solution so obtained, with an isotonic solution or water to a desired concentration.

81. (previously presented) The pharmaceutical composition as claimed in claim 50 in the form of a lotion, oral rinse or toothpaste, wherein the carrier, diluent, excipient or solvent is one acceptable for use in lotion, oral rinse or toothpaste.

82. (cancelled)

83. (currently amended) A method of inhibiting the formation of AGE (Advanced Glycation End products) in a mammal which comprises administering an effective amount of a compound of Formula (I)



(I)

or its pharmaceutically acceptable salts in association with a pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

R_1 is $-N(R_7)N(R_7)R_9$;

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl, provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2

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alkyl and SO₂aryl;

m is 0, 1 or 2;

R₃ is selected from the group consisting of R₇, OR₇, N(R₇) (R₁₀), N=C(R₇) (R₁₀),

N(R₇)N(R₇)(R₁₀), N(R₇) N=C(R₇) (R₁₀) and CH(R₇)C(O)R₈

where R₈ is selected from the group consisting of R₇, OR₇ and NR₇R₁₀;

R₉ is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, C(O)R₁₀, -SO₂R₁₀, C(S)NHR₁₀, C(NH) NH (R₁₀) and C(O) NHR₁₀;

R₁₀ is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R₇, provided R₁₀ may be the same or different for R₁ and R₃ in the same compound;

*B!
cont* X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF₄⁻ and PF₆⁻;

wherein the heteroaryl as defined for R₃ and R₁₀ has heteroatoms selected from the group consisting of O, N and S, wherein the hetroaryl may be substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, C₁-C₆ straight chain or branched alkyl group, and nitro group;

with proviso that,

(i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;

(ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;

- (iii) when R_3 is OR_7 and R_1 is $-NHNH_2$ then R_7 is not alkyl;
- (iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and
- (v) at least one heteroaryl group is present.

84. (previously presented) The method as claimed in claim 83, wherein said compound is selected from the group consisting of:

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,
- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,
- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or

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other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof,

By cont,
(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

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- (ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,
- (av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,
- (ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,
- (bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]

hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

85. (previously presented) A pharmaceutical composition for inhibiting the formation of AGE in a mammal comprising the compounds as defined in claim 83 in association with pharmaceutically acceptable carrier, diluent, excipient or solvent.

86. (currently amended) The composition as claimed in claim 85, wherein said compound is selected from the group ~~comprising~~ consisting of:

(a) N,N'-bis[3-carbonyl-1-(2-thien -2'- yl -2-oxoethyl) -3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(b) 1-(2-ethoxy -2-oxoethyl) -3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,

(f) 1-(2-thien -2'-yl -2-oxoethyl) -3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium

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bromide or other pharmaceutically acceptable salts thereof,

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof,

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-

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oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

B1 cont. (av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium

bromide or other pharmaceutically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.

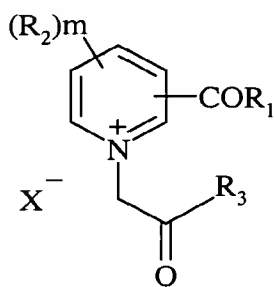
87. (previously presented) A method of inhibiting diseases caused by onset of AGE (Advanced Glycation End products) in a mammal which comprises administering an effective amount of said compound as defined in claim 83 or its pharmaceutically acceptable salts in association with a pharmaceutically acceptable carrier, diluent, excipient or solvent.

88. (currently amended) The method as claimed in claim 87 wherein the diseases which are inhibited are ~~selected from~~ at least one selected from the group consisting of the following group:

- a. vascular and neuro-vascular complications,
- b. nephrological disorder,
- c. neurological disorder,
- d. atherosclerosis,
- e. retinal disorder,

- f. dermatological disorder,
- g. non-enzymatic browning of oral cavity,
- h. endothelial or other organ dysfunction ,
- i. growth impairment,
- j. inflammatory disorder,
- k. immunological disorder,
- l. oxidative stress,
- m. aging and diabetic complication,
- n. alzheimer disease,
- o. restenosis and
- p. erectile dysfunction

B1 cont.
89. (currently amended) A method of treating a mammal for conditions requiring simultaneous action of an AGE-breaker, AGE-formation inhibitor and a free radical scavenger which comprise administering an effective amount of a compound of formula (I)



(I)

or its pharmaceutically acceptable salts, in association with a pharmaceutically acceptable

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carrier, diluent, excipient or solvent,

wherein

R_1 is $-N(R_7)N(R_7)R_9$;

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$, $N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, $-SO_2R_{10}$, $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- and PF_6^- ;

wherein the heteroaryl as defined for R_3 and R_{10} has heteroatoms selected from the group

consisting of O, N and S, wherein the heteroaryl may be substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, C₁-C₆ straight chain or branched alkyl group, and nitro group;

with proviso that,

- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl;
- (iv) when R₃ is OR₇, R₁ is N(R₇)N(R₇)R₉ and R₉ is C(O)R₁₀ where R₁₀ is alkyl, then R₇ is not hydrogen; and
- (v) at least one heteroaryl group is present.

90. (previously presented) The method as claimed in claim 89, wherein said compound is selected from the group consisting of:

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

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(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof,

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

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(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

B1 cont (as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

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(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide
or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium
bromide or other pharmaceutically acceptable salts thereof,

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
chloride or other pharmaceutically acceptable salts thereof,

*B¹
cancel.*
(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]
hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other
pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium
bromide or other pharmaceutically acceptable salts thereof.
